Texas Medicaid/CHIP Vendor Drug Program
Drug Utilization Criteria For Outpatient Use Guidelines
Hydrocodone Bitartrate/Hydrocodone Polistirex

About
Information on indications for use or diagnosis is assumed to be unavailable. All criteria may be applied retrospectively; prospective application is indicated with an asterisk [*]. The information contained is for the convenience of the public. The Texas Health and Human Services Commission is not responsible for any errors in transmission or any errors or omissions in the document.

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1. Dosage [*]

In August 2014, the Drug Enforcement Administration published a final ruling to reschedule hydrocodone combination products from Schedule III to Schedule II due to their high potential of abuse. Effective October 6th, 2014, all hydrocodone combination products will be Schedule II. *Single-entity hydrocodone products were already classified as Schedule II.*

Hydrocodone bitartrate, as combination therapy, is FDA-approved as an opioid antitussive and analgesic used for the relief of cough and moderate to moderately severe pain. Hydrocodone bitartrate is available in fixed combinations with non-opiate drugs (e.g., acetaminophen, acetylsalicylic acid, ibuprofen, chlorpheniramine, phenylephrine, pseudoephedrine, guaifenesin). This drug should be given in the smallest effective dose and as infrequently as possible to minimize the development of tolerance and physical dependence.

Hydrocodone bitartrate has recently become available in the United States as a single entity, extended-release capsule (Zohydro® ER), **formulated with abuse-deterrent beads**. This hydrocodone product is FDA-approved for managing pain requiring daily, long-term, around-the-clock opiate therapy not responsive to other treatment options. **Hydrocodone bitartrate extended-release tablets with abuse deterrent properties (Hysingla® ER) have also been FDA-approved to manage severe pain requiring chronic, around-the-clock opiate treatment unresponsive to other treatment regimens.**

The use of hydrocodone when prescribed by multiple physicians will be reviewed.

Hydrocodone/acetaminophen combination products containing greater than 325 mg of acetaminophen have been discontinued due to liver toxicity. FDA advises health care professionals to discontinue prescribing acetaminophen in strengths higher than 325 mg. If any products containing more than 325 mg of acetaminophen remain on the shelf, pharmacists are encouraged to return them to the manufacturers.

Adults
Analgesic hydrocodone dosages should be determined based on pain severity and patient response/ tolerance. In individuals with severe pain or those who have become tolerant to the analgesic effects of hydrocodone, it may be necessary to exceed the usual dosage. Reduced hydrocodone dosages are indicated in high-risk patients and the elderly. The maximum daily dosage for the acetaminophen/ hydrocodone combination is restricted by the maximum acetaminophen dose of 4 g daily to limit the risk of hepatic damage and severe hypersensitivity reactions associated with acetaminophen use.

Hydrocodone exerts antitussive effects by directly acting on receptors in the cough center at dosages lower than those required for analgesia.

Recommended adult hydrocodone dosages are summarized in Table 1. Dosages exceeding these recommendations will be reviewed.

Table 1: Recommended Adult Hydrocodone Dosages

Drug/Indication	Dosage Forms/Strengths	Usual Dosage Regimen	Maximum Recommended Dose
Single-entity products			
Analgesic hydrocodone extended-release capsule (Zohydro® ER)	**10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 50 mg extended-release, abuse-deterrent capsules**	20 mg to 100 mg every 12 hours	maximum dose not defined; doses should be titrated per patient to maximize analgesia and minimize adverse drug reactions
Analgesic **hydrocodone extended-release tablet (Hysingla® ER)**	**20 mg, 30 mg, 40 mg, 60 mg, 80 mg, 100 mg, 120 mg extended-release, abuse-deterrent tablets**	**20 mg to 120 mg every 24 hours**	**maximum dose not defined; doses should be titrated per patient to maximize analgesia and minimize adverse drug reactions**
Combination products			
Analgesic hydrocodone bitartrate/acetaminophen (Lortab®, Norco®, Vicodin®, generics)	**5 mg/300 mg, 7.5 mg/300 mg, 10 mg/300 mg, 2.5 mg/325 mg, 5 mg/325 mg, 7.5 mg/325 mg, 10 mg/325 mg tablets; 7.5 mg/325 mg/15 ml or 10 mg/325 mg/15 ml solution; 10 mg/300 mg/15 ml elixir**	2.5-10 mg every 4-6 hours as needed	60 mg/4000 mg daily*
hydrocodone bitartrate/ibuprofen (Vicoprofen®, Ibudone®, Reprexain®, generics)	**2.5 mg/200 mg, 5 mg/200 mg, 7.5 mg/200 mg, 10 mg/200 mg tablets**	2.5-10 mg every 4-6 hours as needed	5 tablets per day [maximum hydrocodone dose (10mg/200 mg): 50 mg daily]**
Antitussive hydrocodone bitartrate (in various combinations)	**2.5 mg/5 ml or 5 mg/5 ml solution or 5 mg as tablet in combination products**	5 mg every 4-6 hours as needed	single dose: 15 mg total daily dose: 20 mg to 30 mg
hydrocodone polistirex/ chlorpheniramine polistirex (Tussionex® Pennkinetic®, generics)	**10 mg/8 mg/5 ml extended-release oral suspension**	10 mg/8 mg every 12 hours	20 mg/16 mg daily

**dosage limit based on maximum acetaminophen daily dose; varies by product*
***short-term use (<10 days) recommended*

Pediatrics
Hydrocodone is not FDA-approved for use as an antitussive in pediatric patients younger than 6 years of age as safety and efficacy have not been established. For analgesia, safety and efficacy of the hydrocodone/acetaminophen combination have not been established in children younger than 2 years of age, while the hydrocodone/ibuprofen combination is not indicated for use in children younger than 16 years of age due to lack of safety and efficacy data. **The hydrocodone single-entity products, Zohydro® ER and Hysingla® ER are not FDA-approved in the pediatric population (< 18 years of age) as safety and efficacy in this age group have not been established.**

Analgesic hydrocodone dosages should be determined based on pain severity and patient response/ tolerance. In individuals with severe pain or those who have become tolerant to the analgesic effects of hydrocodone, it may be necessary to exceed the usual dosage. Reduced hydrocodone dosages are indicated in very young patients. Like adult patients, the maximum daily dosage for the acetaminophen/ hydrocodone combination is restricted by the maximum acetaminophen dose (as determined by age and weight – see Table 2) to limit the risk of hepatic damage and severe hypersensitivity reactions associated with acetaminophen use.

Recommended pediatric hydrocodone dosages are summarized in Table 2. Dosages exceeding these recommendations will be reviewed.

Table 2: Recommended Pediatric Hydrocodone Dosages		
Drug/Indication	**Usual Dosage Regimen**	**Maximum Recommended Dose**
Analgesic hydrocodone bitartrate/acetaminophen (APAP) (Lortab®, Norco®, Vicodin®, generics)	***~2-3 years of age*** *(12 to 15 kg):* ~1.875 mg every 4-6 hours as needed	750 mg daily (APAP[+])*
	~4-6 years of age *(16 to 22 kg):* 2.5 mg every 4-6 hours as needed	1 g daily (APAP)*
	~7-9 years of age *(23 to 31 kg):* ~3.75 mg every 4-6 hours as needed	1.5 g daily (APAP)*
	~10-13 years of age *(32 to 45 kg):* 5 mg every 4-6 hours as needed	2 g daily (APAP)*
	≥ 14 years of age *(≥ 46kg):* ~7.5 mg every 4-6 hours as needed	3 g daily (APAP)*
hydrocodone bitartrate/ibuprofen (Vicoprofen®, Ibudone®, Reprexain®, generics)	*16 years and older:* 2.5-10 mg/200 mg every 4-6 hours as needed	5 tablets daily**
Antitussive **hydrocodone bitartrate/ homatropine (Hydromet®, generics)**	***5 mg/1.5 mg/5ml solution or 5 mg/1.5 mg tablet*** *6-12 years of age:* 2.5 mg every 4-6 hours as needed	15 mg daily
	> 12 years of age: 5 mg every 4-6 hours as needed	30 mg daily
hydrocodone polistirex/ chlorpheniramine polistirex (Tussionex® Pennkinetic®, generics)	*6-11 years of age:* 5 mg/4mg every 12 hours	10 mg/8 mg daily
	≥12 years of age: 10 mg/8 mg every 12 hours	20 mg/16 mg daily

[+]*APAP = acetaminophen*
**dosage limit based on maximum acetaminophen daily dose*
***short-term use (<10 days) recommended*

2. **Duration of Therapy**

When used as an analgesic, there is no basis for limiting hydrocodone therapy duration as hydrocodone may be utilized to manage chronic painful conditions as well as acute pain events. As an antitussive, hydrocodone is prescribed for a limited duration to manage cough and upper respiratory symptoms associated with the common cold or allergies in adults and pediatric patients 6 years of age and older. In isolated cases, hydrocodone may be prescribed for an extended time period in those adult patients requiring nonspecific therapy for a chronic, nonproductive cough, such as advanced cancer. In all patients, the smallest effective hydrocodone dose should be administered as infrequently as possible to minimize the development of tolerance and physical dependence.

3.* **Drug-Drug Interactions**

Patient profiles will be assessed to identify those drug regimens which may result in clinically significant drug-drug interactions. Drug-drug interactions considered clinically relevant for hydrocodone are summarized in Table 3. Only those drug-drug interactions classified as clinical significance level 1/contraindicated or those considered life-threatening which have not yet been classified will be reviewed:

Table 3: Hydrocodone Drug-Drug Interactions				
Target Drug	**Interacting Drug**	**Interaction**	**Recommendation**	**Clinical Significance***
hydrocodone	**anticholinergics (e.g., antidiarrheals)**	**co-administration may lead increased risk of urination retention, severe constipation, including paralytic ileus, especially with chronic use, and CNS depression due to additive anticholinergic effects**	**observe for chronic constipation, urinary retention, and CNS depression; adjust doses and/or discontinue therapy as needed**	**2-major (CP)**
hydrocodone	CNS depressants (e.g., anxiolytics, sedatives, tricyclic antidepressants)	adjunctive administration may result in additive CNS and respiratory depression	monitor for additive pharmacologic/adverse effects and reduce drug dosages as necessary	major (DrugReax) 2-major (CP)
hydrocodone	CYP2D6 inhibitors (e.g., amiodarone, fluoxetine, paroxetine, bupropion, ritonavir)	hydrocodone is converted to hydromorphone, an active metabolite that also possesses analgesic effects, through CYP2D6; concurrent administration with CYP2D6 inhibitors may result in increased hydrocodone serum levels and reduced hydromorphone levels and the potential for enhanced or diminished pharmacologic/ adverse effects	monitor for effective analgesia and signs/symptoms of adverse effects (e.g., enhanced sedation, respiratory depression); modify doses as necessary	3-moderate (CP)
hydrocodone	CYP3A4 inducers (e.g., rifampin, barbiturates)	adjunctive use may result in decreased hydrocodone plasma levels/reduced therapeutic effects, including withdrawal, as hydrocodone is CYP3A4 substrate	monitor for effective therapeutic effects; modify doses as necessary	major (DrugReax) 3-moderate (CP)

Table 3: Hydrocodone Drug-Drug Interactions (continued)				
Target Drug	**Interacting Drug**	**Interaction**	**Recommendation**	**Clinical Significance***
hydrocodone	CYP3A4 inhibitors	concurrent administration with CY3A4 inhibitors may result in increased hydrocodone serum levels and the potential for enhanced pharmacologic/ adverse effects through inhibition of CYP3A4-mediated hydrocodone metabolism	monitor for effective analgesia and signs/symptoms of adverse effects (e.g., enhanced sedation, respiratory depression); modify doses as necessary	major (DrugReax) 2-major (CP)
hydrocodone	MAOIs	combined administration may result in severe, unpredictable additive effects	although no specific adverse interactions have been reported with the hydrocodone-MAOI combination, hydrocodone should not be administered in patients who have received MAOIs within 14 days	major (DrugReax) 2-major (CP)
hydrocodone	OAAs	concomitant administration may result in partial blockade of hydrocodone pharmacologic effects and may precipitate a withdrawal syndrome in some patients requiring chronic hydrocodone therapy; antagonist effects are more likely to occur when OAAs used concurrently with low to moderate doses of a pure opioid agonist; adjunctive therapy may be required in some instances, which may result in additive CNS depressant, respiratory, and hypotensive effects	patients requiring concurrent therapy with hydrocodone and a mixed OAA should be monitored for enhanced or attenuated pharmacologic effects, which may necessitate hydrocodone dosage adjustments and/or pharmacotherapy modifications	major (DrugReax) 2-major (CP)
hydrocodone	OAs	concurrent administration of pure OAs antagonists and narcotic analgesics like hydrocodone, or administration of OAs within 7 to 10 days of narcotic analgesic therapy may induce an acute abstinence syndrome	unless clinically significant respiratory depression is present, OAs should not be administered concurrently with hydrocodone	contraindicated (DrugReax) 2-major (CP)

**CP = Clinical Pharmacology*
CNS = central nervous system; MAOIs = monoamine oxidase inhibitors; OAs = opioid antagonists; OAAs = opioid agonists/antagonists

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